Clinical Policy: Cariprazine (Vraylar)
Reference Number: CP.PMN.91
Effective Date: 11.16.16
Last Review Date: 02.20
Line of Business: Commercial, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Cariprazine (Vraylar®) is an atypical antipsychotic.

FDA Approved Indication(s)
Vraylar is indicated for:
- Treatment of schizophrenia in adults
- Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults
- Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Vraylar is medically necessary when the following criteria are met:

I. Initial Approval Criteria
A. Bipolar Disorder and Schizophrenia (must meet all):
   1. Diagnosis of bipolar disorder or schizophrenia;
   2. Age ≥ 18 years;
   3. Failure of two preferred atypical antipsychotics (e.g., aripiprazole, ziprasidone, quetiapine, risperidone, or olanzapine) at up to maximally indicated doses, each used for ≥ 4 weeks, unless contraindicated or clinically significant adverse effects are experienced;
   4. Dose does not exceed any of the following:
      a. Schizophrenia or manic or mixed episodes of bipolar I disorder: 6 mg (1 capsule) per day;
      b. Depressive episodes of bipolar I disorder: 3 mg (1 capsule) per day.

Approval duration:
Medicaid – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.
II. Continued Therapy
   A. All Indications in Section I (must meet all):
      1. Currently receiving medication via Centene benefit, or documentation supports that
         member is currently receiving Vraylar for bipolar disorder or schizophrenia and has
         received this medication for at least 30 days;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed any of the following:
         a. Schizophrenia or manic or mixed episodes of bipolar I disorder: 6 mg (1 capsule)
            per day;
         b. Depressive episodes of bipolar I disorder: 3 mg (1 capsule) per day.
   Approval duration:
   Medicaid – 12 months
   Commercial – Length of Benefit

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via Centene benefit and documentation supports
         positive response to therapy.
         Approval duration: Duration of request or 12 months (whichever is less); or
      2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT
         specifically listed under section III (Diagnoses/Indications for which coverage is
         NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is
      sufficient documentation of efficacy and safety according to the off label use policies –
      CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage
      documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   FDA: Food and Drug Administration

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval
   criteria. The drugs listed here may not be a formulary agent for all relevant lines of business
   and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>aripiprazole (Abilify®)</td>
<td>Bipolar Disorder and Schizophrenia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adults: 10 to 15 mg PO QD</td>
<td>30 mg/day</td>
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<tr>
<td>olanzapine (Zyprexa®)</td>
<td>Schizophrenia</td>
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<tr>
<td></td>
<td>Initial: 5 to 10 mg PO QD; target: 10 mg PO QD</td>
<td>20 mg/day</td>
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<tr>
<td></td>
<td>Bipolar Disorder</td>
<td></td>
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</tbody>
</table>
CLINICAL POLICY
Cariprazine

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>quetiapine</td>
<td>Monotherapy: 10 to 15 mg PO QD; adjunct to lithium or valproate: 10 mg PO QD</td>
<td>800 mg/day</td>
</tr>
<tr>
<td>(Seroquel®)</td>
<td><strong>Schizophrenia</strong> Initial: 25 mg PO BID; target: 400 to 800 mg/day</td>
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<tr>
<td></td>
<td><strong>Bipolar Disorder</strong> Initial: 50 mg PO BID; target: 400 to 800 mg/day</td>
<td></td>
</tr>
<tr>
<td>risperidone</td>
<td>Schizophrenia Initial: 1 mg PO BID or 2 mg PO QD; target: 4 to 8 mg PO QD</td>
<td>Schizophrenia: 16 mg/day</td>
</tr>
<tr>
<td>(Risperdal®)</td>
<td><strong>Bipolar Disorder</strong> 2 to 3 mg PO QD</td>
<td>Bipolar Disorder: 6 mg/day</td>
</tr>
<tr>
<td>ziprasidone</td>
<td>Schizophrenia 20 mg PO BID</td>
<td>160 mg/day</td>
</tr>
<tr>
<td>(Geodon®)</td>
<td><strong>Bipolar Disorder</strong> Initial: 40 mg PO BID; target: 40 to 80 mg PO BID</td>
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*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to Vraylar
- Boxed warning(s): Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Vraylar is not approved for the treatment of patients with dementia-related psychosis.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>1.5 mg to 6 mg PO QD</td>
<td>6 mg/day</td>
</tr>
</tbody>
</table>
| Bipolar I disorder | Manic or mixed episodes: 3 mg to 6 mg PO QD  
Depressive episodes: 1.5 mg or 3 mg PO QD | Manic or mixed episodes: 6 mg/day  
Depressive episodes: 3 mg/day |

VI. Product Availability
Capsules: 1.5 mg, 3 mg, 4.5 mg, 6 mg

VII. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1Q18 annual review: Policy generated from existing commercial policy – CP.CPA.221; No significant change from previously approved corporate policy; New for Medicaid; Age added for schizophrenia per safety guidance endorsed by Centene Medical Affairs.</td>
<td>11.13.17</td>
<td>02.18</td>
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<tr>
<td>1Q 2019 annual review: no significant changes; references reviewed and updated.</td>
<td>10.30.18</td>
<td>02.19</td>
</tr>
<tr>
<td>RT4: updated policy to add newly FDA-approved indication for depressive episodes associated with bipolar I disorder; references updated.</td>
<td>06.14.19</td>
<td></td>
</tr>
<tr>
<td>1Q 2020 annual review: no significant changes; references reviewed and updated.</td>
<td>11.30.19</td>
<td>02.20</td>
</tr>
</tbody>
</table>

**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and
limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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